LACHMAN CONSULTANT SERVICES, INC.
CONSULTANTS TO THE PHARMACEUTICAL AND ALLIED INDUSTRIES

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February 18, 2005

OVERNIGHT COURIER 2/18/05

Division of Dockets Management
Food and Drug Administration (HFA-305)
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Citizen Petition

Dear Sir or Madam:

The undersigned submits this petition, in quadruplicate, pursuant to Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act, and in accordance with 21 CFR 10.30 on behalf of a client requesting the Commissioner of the Food and Drug Administration to make a determination that the drug product, Prednisolone Sodium Phosphate Solution, in the strengths of 10 mg/5 mL, 20 mg/5 mL and 25 mg/5 mL (equivalent prednisolone base), is suitable for consideration in an abbreviated new drug application (ANDA).

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration make a determination that a Prednisolone Sodium Phosphate Solution, in the strengths 10 mg/5 mL, 20 mg/5 mL and 25 mg/5 mL (of equivalent prednisolone base) is suitable for submission as an ANDA product. The reference-listed drug product (RLD), upon which this petition is based, is Orapred® Oral Solution (prednisolone sodium phosphate solution, 15 mg equivalent prednisolone base per 5 mL) by Ascent Pediatrics. The petitioner seeks a change in strength (of equivalent prednisolone base) from 15 mg/5 mL of the listed drug product to 10 mg/5 mL, 20 mg/5 mL and 25 mg/5 mL.

B. Statement of Grounds

The Federal Food, Drug and Cosmetic Act provides for the submission of an Abbreviated New Drug Application for a drug product that differs in dosage strength from that of the listed drug provided the FDA has approved a petition that proposed filing such an application.

The RLD, Orapred® Oral Solution by Ascent Pediatrics, is a prednisolone sodium phosphate oral solution product containing 15 mg/5 mL equivalent prednisolone base. See listing in the Electronic Orange Book, *Approved Drug Products with Therapeutic Equivalence Evaluations*, current through December 2004 (Attachment 1). The proposed drug product also represents a prednisolone sodium phosphate oral solution dosage form, but proposes to contain the

equivalent prednisolone base in strengths of 10 mg/5 mL, 20 mg/5 mL and 25 mg/5 mL. The petition is thus seeking a change in strength (from 15 mg/5 mL to 10 mg/5 mL, 20 mg/5 mL and 25 mg/5 mL), from that of the RLD. Please note that the proposed changes in strength represent dosage strengths just below and slightly above the currently approved 15 mg/5 mL strength.

The Dosage and Administration section of the approved Reference-Listed Drug labeling states that the initial dosage of the prednisolone sodium phosphate solution will vary from "5 to 60 mg prednisolone base depending on the specific disease entity being treated". It also states (in bold face) the "dosage requirements are variable and must be individualized on the basis of the disease under treatment and the response of the patient". Suggested dosage levels listed for various disease entities in the approved labeling range from 0.14 mg/kg/day in divided doses to 80 mg every other day (see the approved package insert for Orapred® Oral Solution, Attachment 2). The proposed dosage for this product would not differ from that currently approved; it would remain the same as the currently approved RLD labeling with revisions only made to replace equivalent dosage for any previous milliliter administration references (i.e., 20 mL of the currently approved RLD would now be 60 mg eq. prednisolone base). See proposed labeling, (Attachment 3).

As the active ingredient and route of administration will remain the same and the suggested dosage will remain the same as currently approved, the proposed additional strengths will only add greater flexibility and ease to the required dosing of this drug. As stated above, the approved RLD labeling quite clearly indicates that the dosing of such a product can be variable and must be carefully individualized based upon both the patient and disease. The addition of the proposed 10 mg, 20 mg and 25 mg per 5 mL strengths of this product will only add to the ease of product administration and enhance the healthcare practitioner's ability to further optimize individual patient dosage (within the approved dosage parameters) while minimizing potential adverse events that may occur if the improper dose were measured. These alternate strengths will enable the healthcare practitioner to minimize any potential adverse effects by providing a product where dosing is more accurately and more easily attainable for the proposed product based on each individual patient's needs, as determined by the prescriber. In addition, it will give the provider, caregiver or patient the ability to administer the most appropriate dose in a volume that may be more tolerable and easier to dispense and take, than what may be required if only one strength was available. This can be especially significant for higher or lower doses required by specific patients. For a pediatric patient requiring a 2 mg prednisolone dose, it would be much easier to measure and administer 1 mL of a 10 mg/5 mL strength product rather than 0.67mL of a 15 mg/5 mL product. On the opposite end, an 80 mg dose would require only 16 mL of a 25 mg/5 mL strength product, over 10 mL less than would be required of the currently approved 15mg/5mL strength.

There are no other proposed changes in labeling with the exception of the obvious changes in strength sought in this petition. The uses, indications, warnings and directions for use will remain the same as that of the RLD. The RLD's approved labeling is provided in Attachment 2 and draft labeling for the proposed product is included in Attachment 3.

Thus, for the abovementioned reasons, the petitioner's request for the Commissioner to find that a change in strength from 15 mg/5 mL to 10 mg/5 mL, 20 mg/5 mL and 25 mg/5 mL for Prednisolone Sodium Phosphate Oral Solution should raise no questions of safety or effectiveness, and the Agency should approve the petition.

C. Environmental Impact

The petitioner claims a categorical exclusion under 21 CFR 25.31.

D. Economic Impact

The petitioner does not believe that this is applicable in this case, but will agree to provide such an analysis if requested by the Agency.

E. Certification

The undersigned certifies, that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,

Robert W. Pollock
Vice President
Lachman Consultant Services, Inc
1600 Stewart Avenue
Westbury, NY 11590

RWP/bh

cc: Emily Thakur (Office of Generic Drugs)

Attachments:
1. Electronic Orange Book, *Approved Drug Products with Therapeutic Equivalence Evaluations*, current through December 2004
2. Referenced-listed Drug Labeling for Orapred® Oral Solution
3. Proposed Draft Insert Labeling Proposed for Prednisolone Sodium Phosphate Oral Solution

B33p5048

LACHMAN CONSULTANT SERVICES, INC.
Westbury, NY 11590

ATTACHMENT 1

Electronic Orange Book

Approved Drug Products
with
Therapeutic Equivalence Evaluations

Current through December 2004

Preface

FAQ

Search by Active Ingredient **Search by Applicant Holder**

Search by Proprietary Name **Search by Application Number**

Search by Patent NEW!!

The products in this list have been approved under section 505 of the Federal Food, Drug, and Cosmetic Act.

Drug questions email: DRUGINFO@CDER.FDA.GOV

U.S Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Pharmaceutical Science
Office of Generic Drugs

Active Ingredient Search Results from "OB_Rx" table for query on "Prednisolone Sodium Phosphate."

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
040065	AT	No	PREDNISOLONE SODIUM PHOSPHATE	SOLUTION/DROPS; OPHTHALMIC	EQ 0.11% PHOSPHATE	PREDNISOLONE SODIUM PHOSPHATE	BAUSCH AND LOM
040070	AT	No	PREDNISOLONE SODIUM PHOSPHATE	SOLUTION/DROPS; OPHTHALMIC	EQ 0.9% PHOSPHATE	PREDNISOLONE SODIUM PHOSPHATE	BAUSCH AND LOM
080751	AT	Yes	PREDNISOLONE SODIUM PHOSPHATE	SOLUTION/DROPS; OPHTHALMIC	EQ 0.11% PHOSPHATE	INFLAMASE MILD	NOVARTI
080751	AT	Yes	PREDNISOLONE SODIUM PHOSPHATE	SOLUTION/DROPS; OPHTHALMIC	EQ 0.9% PHOSPHATE	INFLAMASE FORTE	NOVARTI
075117	AA	Yes	PREDNISOLONE SODIUM PHOSPHATE	SOLUTION; ORAL	EQ 15MG BASE/5ML	ORAPRED	ASCENT PEDS
019157	AA	Yes	PREDNISOLONE SODIUM PHOSPHATE	SOLUTION; ORAL	EQ 5MG BASE/5ML	PEDIAPRED	CELLTEC PHARMS
075183	AA	No	PREDNISOLONE SODIUM PHOSPHATE	SOLUTION; ORAL	EQ 5MG BASE/5ML	PREDNISOLONE SODIUM PHOSPHATE	HI TECH PHARMA
076895	AA	No	PREDNISOLONE SODIUM PHOSPHATE	SOLUTION; ORAL	EQ 15MG BASE/5ML	PREDISOLONE SODIUM PHOSPHATE	MORTON GROVE
075099	AA	No	PREDNISOLONE SODIUM PHOSPHATE	SOLUTION; ORAL	EQ 5MG BASE/5ML	PREDNISOLONE SODIUM PHOSPHATE	MORTON GROVE
075988	AA	No	PREDNISOLONE SODIUM PHOSPHATE	SOLUTION; ORAL	EQ 5MG BASE/5ML	PREDNISOLONE SODIUM PHOSPHATE	PADDOCI
076123	AA	No	PREDNISOLONE SODIUM PHOSPHATE	SOLUTION; ORAL	EQ 5MG BASE/5ML	PREDNISOLONE SODIUM PHOSPHATE	PHARM ASSOC
075250	AA	No	PREDNISOLONE SODIUM PHOSPHATE	SOLUTION; ORAL	EQ 15MG BASE/5ML	PREDNISOLONE SODIUM PHOSPHATE	WE PHARMS

075181	AA	No	PREDNISOLONE SODIUM PHOSPHATE	SOLUTION; ORAL	EQ 5MG BASE/5ML	PREDNISOLONE SODIUM PHOSPHATE	WE PHARMS
073630	AT	No	PREDNISOLONE SODIUM PHOSPHATE; SULFACETAMIDE SODIUM	SOLUTION/DROPS; OPHTHALMIC	EQ 0.23% PHOSPHATE;10%	SULFACETAMIDE SODIUM AND PREDNISOLONE SODIUM PHOSPHATE	ALCON
074449	AT	No	PREDNISOLONE SODIUM PHOSPHATE; SULFACETAMIDE SODIUM	SOLUTION/DROPS; OPHTHALMIC	EQ 0.23% PHOSPHATE;10%	SULFACETAMIDE SODIUM AND PREDNISOLONE SODIUM PHOSPHATE	BAUSCH AND LOM
018988	AT	Yes	PREDNISOLONE SODIUM PHOSPHATE; SULFACETAMIDE SODIUM	SOLUTION/DROPS; OPHTHALMIC	EQ 0.23% PHOSPHATE;10%	VASOCIDIN	NOVARTI

Return to Electronic Orange Book Home Page

FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:

Orange Book Data - **Monthly**

Orange Book Data Updated Through December, 2004

Orange Book Patent Data Only - **Daily**

Patent Data Last Updated: February 17, 2005

Search results from the "OB_Rx" table for query on "075117."

Active Ingredient:	PREDNISOLONE SODIUM PHOSPHATE
Dosage Form;Route:	SOLUTION; ORAL
Proprietary Name:	ORAPRED
Applicant:	ASCENT PEDS
Strength:	EQ 15MG BASE/5ML
Application Number:	075117
Product Number:	001
Approval Date:	Dec 14, 2000
Reference Listed Drug	Yes
RX/OTC/DISCN:	RX
TE Code:	**AA**
Patent and Exclusivity Info for this product:	View

Return to Electronic Orange Book Home Page

FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Orange Book Data Updated Through December, 2004
Orange Book Patent Data Only - **Daily**
Patent Data Last Updated: February 17, 2005

LACHMAN CONSULTANT SERVICES, INC.
Westbury, NY 11590

ATTACHMENT 2

Orapred®

(prednisolone sodium phosphate oral solution)

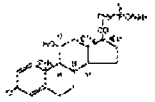
Rx only

DESCRIPTION

Orapred Solution is a dye free, pale to light yellow solution Each 5 mL (teaspoonful) of Orapred contains 20 2 mg prednisolone sodium phosphate (15 mg prednisolone base) in a palatable, aqueous vehicle

Inactive Ingredients: Orapred Solution equivalent to 15 mg prednisolone per 5 mL contains the following inactive ingredients alcohol 2%, fructose, glycerin, monoammonium glycyrrhizinate, povidone, sodium benzoate, sorbitol, and flavor Orapred may contain citric acid and/or sodium hydroxide for pH adjustment

Prednisolone sodium phosphate occurs as white or slightly yellow, friable granules or powder It is freely soluble in water, soluble in methanol, slightly soluble in alcohol and in chloroform, and very slightly soluble in acetone and in dioxane The chemical name of prednisolone sodium phosphate is pregna-1,4-diene-3,20-dione,11,17-dihydroxy-21-(phosphonooxy)-, disodium salt, (11ß)- The empirical formula is $C_{21}H_{27}Na_2O_8P$, the molecular weight is 484 39 Its chemical structure is



Pharmacological Category Glucocorticoid

CLINICAL PHARMACOLOGY

Naturally occurring glucocorticoids (hydrocortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states Their synthetic analogs are primarily used for their potent anti-inflammatory effects in disorders of many organ systems

Prednisolone is a synthetic adrenocortical steroid drug with predominantly glucocorticoid properties Some of these properties reproduce the physiological actions of endogenous glucocorticosteroids, but others do not necessarily reflect any of the adrenal hormones' normal functions, they are seen only after administration of large therapeutic doses of the drug The pharmacological effects of prednisolone which are due to its glucocorticoid properties include: promotion of gluconeogenesis, increased deposition of glycogen in the liver; inhibition of the utilization of glucose; anti-insulin activity; increased catabolism of protein, increased lipolysis, stimulation of fat synthesis and storage; increased glomerular filtration rate and resulting increase in urinary excretion of urate (creatinine excretion remains unchanged), and increased calcium excretion

Depressed production of eosinophils and lymphocytes occurs, but erythropoiesis and production of polymorphonuclear leukocytes are stimulated Inflammatory processes (edema, fibrin deposition, capillary dilatation, migration of leukocytes and phagocytosis) and the later stages of wound healing (capillary proliferation, deposition of collagen, cicatrization) are inhibited

Prednisolone can stimulate secretion of various components of gastric juice Suppression of the production of corticotropin may lead to suppression of endogenous corticosteroids Prednisolone has slight mineralocorticoid activity, whereby entry of sodium into cells and loss of intracellular potassium is stimulated This is particularly evident in the kidney, where rapid ion exchange leads to sodium retention and hypertension

Prednisolone is rapidly and well absorbed from the gastrointestinal tract following oral administration Orapred Solution produces a 14% higher peak plasma level of prednisolone which occurs 20% faster than the peak seen with tablets. Prednisolone is 70-90% protein-bound in the plasma and it is eliminated from the plasma with a half-life of 2 to 4 hours. It is metabolized mainly in the liver and excreted in the urine as sulfate and glucuronide conjugates

INDICATIONS AND USAGE

Orapred Solution is indicated in the following conditions

1. Endocrine Disorders

Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the first choice, synthetic analogs may be used in conjunction with mineralocorticoids where applicable, in infancy mineralocorticoid supplementation is of particular importance), congenital adrenal hyperplasia; hypercalcemia associated with cancer, nonsuppurative thyroiditis

2. Rheumatic Disorders

As adjunctive therapy for short term administration (to tide the patient over an acute episode or exacerbation) in psoriatic arthritis, rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low dose maintenance therapy); ankylosing spondylitis, acute and subacute bursitis, acute nonspecific tenosynovitis, acute gouty arthritis, epicondylitis For the treatment of systemic lupus erythematosus, dermatomyositis (polymyositis), polymyalgia rheumatica, Sjogren's syndrome, relapsing polychondritis, and certain cases of vasculitis

3. Dermatologic Diseases

Pemphigus, bullous dermatitis herpetiformis; severe erythema multiforme (Stevens-Johnson syndrome), exfoliative erythroderma, mycosis fungoides

4. Allergic States

Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in adult and pediatric populations with: seasonal or perennial allergic rhinitis, asthma, contact dermatitis; atopic dermatitis, serum sickness, drug hypersensitivity reactions

5. Ophthalmic Diseases

Uveitis and ocular inflammatory conditions unresponsive to topical corticosteroids, temporal arteritis, sympathetic ophthalmia

6. Respiratory Diseases

Symptomatic sarcoidosis; idiopathic eosinophilic pneumonias, fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy, asthma (as distinct from allergic asthma listed above under "Allergic States"), hypersensitivity pneumonitis, idiopathic pulmonary fibrosis, acute exacerbations of chronic obstructive pulmonary disease (COPD), and Pneumocystis carinii pneumonia (PCP) associated with hypoxemia occurring in an HIV (+) individual who is also under treatment with appropriate anti-PCP antibiotics. Studies support the efficacy of systemic corticosteroids for the treatment of these conditions allergic bronchopulmonary aspergillosis, idiopathic bronchiolitis obliterans with organizing pneumonia

7. Hematologic Disorders

Idiopathic thrombocytopenic purpura in adults, selected cases of secondary thrombocytopenia, acquired (autoimmune) hemolytic anemia, pure red cell aplasia, Diamond-Blackfan anemia

8. Neoplastic Diseases

For the treatment of acute leukemia and aggressive lymphomas in adults and children

9. Edematous States

To induce diuresis or remission of proteinuria in nephrotic syndrome in adults with lupus erythematosus and in adults and pediatric populations, with idiopathic nephrotic syndrome, without uremia

10. Gastrointestinal Diseases

To tide the patient over a critical period of the disease in ulcerative colitis, regional enteritis

11. Nervous System

Acute exacerbations of multiple sclerosis

12. Miscellaneous

Tuberculous meningitis with subarachnoid block or impending block, tuberculosis with enlarged mediastinal lymph nodes causing respiratory difficulty, and tuberculosis with pleural or pericardial effusion (appropriate antituberculous chemotherapy must be used concurrently when treating any tuberculosis complications), trichinosis with neurologic or myocardial involvement, acute or chronic solid organ rejection (with or without other agents)

CONTRAINDICATIONS

Systemic fungal infections

Hypersensitivity to the drug or any of its components

WARNINGS

General:

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation is indicated

Endocrine:

Corticosteroids can produce reversible hypothalamic-pituitary adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment

Metabolic clearance of corticosteroids is decreased in hypothyroid patients and increased in hyperthyroid patients Changes in thyroid status of the patient may necessitate adjustment in dosage

Infections (general):

Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals There may be decreased resistance and inability to localize infection when corticosteroids are used. Infection with any pathogen including viral, bacterial, fungal, protozoan or helminthic infection, in any location of the body, may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents that affect humoral or cellular immunity, or neutrophil function These infections may be mild to severe, and, with increasing doses of corticosteroids, the rate of occurrence of infectious complications increases Corticosteroids may also mask some signs of infection after it has already started

Viral infections:

Chicken pox and measles for example, can have a more serious or even fatal course in non-immune children or adults on corticosteroids. In such children or adults who have not had the diseases, particular care should be taken to avoid exposure. How the dose, route and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known If exposed to chicken pox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated If exposed to measles, prophylaxis with immunoglobulin (IG) may be indicated (See the respective package inserts for complete VZIG and IG prescribing information) If chicken pox develops, treatment with antiviral agents should be considered

Special pathogens:

Latent disease may be activated or there may be an exacerbation of intercurrent infections due to pathogens, including those caused by Candida, Mycobacterium, Ameba, Toxoplasma, Pneumocystis, Cryptococcus, Nocardia, etc.

Corticosteroids may activate latent amebiasis. Therefore, it is recommended that latent or active amebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or in any patient with unexplained diarrhea

Similarly, corticosteroids should be used with great care in patients with known or suspected Strongyloides (threadworm) infestation. In such patients, corticosteroid-induced immunosuppression may lead to Strongyloides hyperinfection and dissemination with widespread larval migration, often accompanied by severe enterocolitis and potentially fatal gram-negative septicemia.

Corticosteroids should not be used in cerebral malaria

Tuberculosis:

The use of prednisolone in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen.

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur During prolonged corticosteroid therapy these patients should receive chemoprophylaxis

Vaccination:

Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered, however, the response to such vaccines can not be predicted. Immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e g , for Addison's disease

Ophthalmic:

Use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to bacteria, fungi or viruses The use of oral corticosteroids is not recommended in the treatment of optic neuritis and may lead to an increase in the risk of new episodes. Corticosteroids should not be used in active ocular herpes simplex

Cardio-renal:

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium These effects are less likely to occur with the synthetic derivatives except when used in large doses Dietary salt restriction and potassium supplementation may be necessary All corticosteroids increase calcium excretion

PRECAUTIONS

General:

The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should be gradual

Since complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment, a risk/benefit decision must be made in each individual case as to dose and duration of treatment and as to whether daily or intermittent therapy should be used

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis

Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy, most often for chronic conditions. Discontinuation of corticosteroids may result in clinical improvement.

Endocrine:

Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

Ophthalmic:

Intraocular pressure may become elevated in some individuals If steroid therapy is continued for more than 6 weeks, intraocular pressure should be monitored

Neuro-psychiatric:

Although controlled clinical trials have shown corticosteroids to be effective in speeding the resolution of acute exacerbations of multiple sclerosis, they do not show that they affect the ultimate outcome or natural history of the disease The studies do show that relatively high doses of corticosteroids are necessary to demonstrate a significant effect. (See DOSAGE AND ADMINISTRATION)

An acute myopathy has been observed with the use of high doses of corticosteroids, most often occurring in patients with disorders of neuromuscular transmission (e.g., myasthenia gravis), or in patients receiving concomitant therapy with neuromuscular blocking drugs (e g , pancuronium) This acute

Orapred®
(prednisolone sodium phosphate oral solution)
45502-088

Orapred®
(prednisolone sodium phosphate oral solution)
45502-088

LACHMAN CONSULTANT SERVICES, INC.
Westbury, NY 11590

ATTACHMENT 3

Prednisolone Sodium Phosphate Oral Solution (10mg/5mL, 20mg/5mL and 25 mg/5mL equivalent)

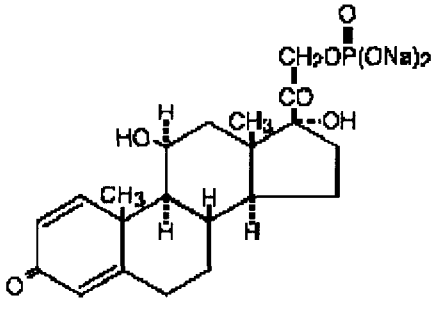
Rx only

DESCRIPTION

Prednisolone Sodium Phosphate Oral Solution is a dye free, pale to light yellow solution. It is available in three strengths in which each 5 mL (teaspoonful) of Prednisolone Sodium Phosphate Oral Solution contains 13.5 mg, 26.9 mg or 33.7 mg prednisolone sodium phosphate (equivalent to 10 mg, 20 mg or 25 mg prednisolone base respectively) in a palatable, aqueous vehicle.

Inactive Ingredients: *Information on the inactive ingredients to be provided when the ANDA is submitted.*

Prednisolone sodium phosphate occurs as white or slightly yellow, friable granules or powder. It is freely soluble in water; soluble in methanol; slightly soluble in alcohol and in chloroform; and very slightly soluble in acetone and in dioxane. The chemical name of prednisolone sodium phosphate is pregna-1,4-diene-3,20-dione,11,17-dihydroxy-21-(phosphonooxy)-, disodium salt, (11ß)-. The empirical formula is $C_{21}H_{27}Na_2O_8P$; the molecular weight is 484.39. Its chemical structure is:



Pharmacological Category: Glucocorticoid

CLINICAL PHARMACOLOGY

Naturally occurring glucocorticoids (hydrocortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs are primarily used for their potent anti-inflammatory effects in disorders of many organ systems.

Prednisolone is a synthetic adrenocortical steroid drug with predominantly glucocorticoid properties. Some of these properties reproduce the physiological actions of endogenous glucocorticosteroids, but others do not necessarily reflect any of the adrenal hormones' normal functions; they are seen only after administration of large therapeutic doses of the drug. The pharmacological effects of prednisolone which are due to its glucocorticoid properties include: promotion of gluconeogenesis; increased deposition of glycogen in the liver; inhibition of the utilization of glucose; anti-insulin activity; increased catabolism of protein; increased lipolysis;

stimulation of fat synthesis and storage; increased glomerular filtration rate and resulting increase in urinary excretion of urate (creatinine excretion remains unchanged); and increased calcium excretion.

Depressed production of eosinophils and lymphocytes occurs, but erythropoiesis and production of polymorphonuclear leukocytes are stimulated. Inflammatory processes (edema, fibrin deposition, capillary dilatation, migration of leukocytes and phagocytosis) and the later stages of wound healing (capillary proliferation, deposition of collagen, cicatrization) are inhibited.

Prednisolone can stimulate secretion of various components of gastric juice. Suppression of the production of corticotropin may lead to suppression of endogenous corticosteroids. Prednisolone has slight mineralocorticoid activity, whereby entry of sodium into cells and loss of intracellular potassium is stimulated. This is particularly evident in the kidney, where rapid ion exchange leads to sodium retention and hypertension.

Prednisolone is rapidly and well absorbed from the gastrointestinal tract following oral administration. Prednisolone Sodium Phosphate Oral Solution produces a 14% higher peak plasma level of prednisolone which occurs 20% faster than the peak seen with tablets. Prednisolone is 70-90% protein-bound in the plasma and it is eliminated from the plasma with a half-life of 2 to 4 hours. It is metabolized mainly in the liver and excreted in the urine as sulfate and glucuronide conjugates.

INDICATIONS AND USAGE

Prednisolone Sodium Phosphate Oral Solution is indicated in the following conditions:

1. Endocrine Disorders

Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the first choice; synthetic analogs may be used in conjunction with mineralocorticoids where applicable; in infancy mineralocorticoid supplementation is of particular importance); congenital adrenal hyperplasia; hypercalcemia associated with cancer; nonsuppurative thyroiditis.

2. Rheumatic Disorders

As adjunctive therapy for short term administration (to tide the patient over an acute episode or exacerbation) in: psoriatic arthritis; rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low dose maintenance therapy); ankylosing spondylitis; acute and subacute bursitis; acute nonspecific tenosynovitis; acute gouty arthritis; epicondylitis. For the treatment of systemic lupus erythematosus, dermatomyositis (polymyositis), polymyalgia rheumatica, Sjogren's syndrome, relapsing polychondritis, and certain cases of vasculitis.

3. Dermatologic Diseases

Pemphigus; bullous dermatitis herpetiformis; severe erythema multiforme (Stevens-Johnson syndrome); exfoliative erythroderma; mycosis fungoides.

4. Allergic States

Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in adult and pediatric populations with: seasonal or perennial allergic

rhinitis; asthma; contact dermatitis; atopic dermatitis; serum sickness; drug hypersensitivity reactions.

5. Ophthalmic Diseases
Uveitis and ocular inflammatory conditions unresponsive to topical corticosteroids; temporal arteritis; sympathetic ophthalmia.

6. Respiratory Diseases
Symptomatic sarcoidosis; idiopathic eosinophilic pneumonias; fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy; asthma (as distinct from allergic asthma listed above under "Allergic States"), hypersensitivity pneumonitis, idiopathic pulmonary fibrosis, acute exacerbations of chronic obstructive pulmonary disease (COPD), and Pneumocystis carinii pneumonia (PCP) associated with hypoxemia occurring in an HIV (+) individual who is also under treatment with appropriate anti-PCP antibiotics. Studies support the efficacy of systemic corticosteroids for the treatment of these conditions: allergic bronchopulmonary aspergillosis, idiopathic bronchiolitis obliterans with organizing pneumonia.

7. Hematologic Disorders
Idiopathic thrombocytopenic purpura in adults; selected cases of secondary thrombocytopenia; acquired (autoimmune) hemolytic anemia; pure red cell aplasia; Diamond-Blackfan anemia.

8. Neoplastic Diseases
For the treatment of acute leukemia and aggressive lymphomas in adults and children.

9. Edematous States
To induce diuresis or remission of proteinuria in nephrotic syndrome in adults with lupus erythematosus and in adults and pediatric populations, with idiopathic nephrotic syndrome, without uremia.

10. Gastrointestinal Diseases
To tide the patient over a critical period of the disease in: ulcerative colitis; regional enteritis.

11. Nervous System
Acute exacerbations of multiple sclerosis.

12. Miscellaneous
Tuberculous meningitis with subarachnoid block or impending block, tuberculosis with enlarged mediastinal lymph nodes causing respiratory difficulty, and tuberculosis with pleural or pericardial effusion (appropriate antituberculous chemotherapy must be used concurrently when treating any tuberculosis complications); trichinosis with neurologic or myocardial involvement; acute or chronic solid organ rejection (with or without other agents).

CONTRAINDICATIONS
Systemic fungal infections.
Hypersensitivity to the drug or any of its components.

WARNINGS

General:

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation is indicated.

Endocrine:

Corticosteroids can produce reversible hypothalamic-pituitary adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment.

Metabolic clearance of corticosteroids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in dosage.

Infections (general):

Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. There may be decreased resistance and inability to localize infection when corticosteroids are used. Infection with any pathogen including viral, bacterial, fungal, protozoan or helminthic infection, in any location of the body, may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents that affect humoral or cellular immunity, or neutrophil function. These infections may be mild to severe, and, with increasing doses of corticosteroids, the rate of occurrence of infectious complications increases. Corticosteroids may also mask some signs of infection after it has already started.

Viral infections:

Chicken pox and measles for example, can have a more serious or even fatal course in non-immune children or adults on corticosteroids. In such children or adults who have not had the diseases, particular care should be taken to avoid exposure. How the dose, route and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chicken pox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information). If chicken pox develops, treatment with antiviral agents should be considered.

Special pathogens:

Latent disease may be activated or there may be an exacerbation of intercurrent infections due to pathogens, including those caused by Candida, Mycobacterium, Ameba, Toxoplasma, Pneumocystis, Cryptococcus, Nocardia, etc.

Corticosteroids may activate latent amebiasis. Therefore, it is recommended that latent or active amebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or in any patient with unexplained diarrhea.

Similarly, corticosteroids should be used with great care in patients with known or suspected Strongyloides (threadworm) infestation. In such patients, corticosteroid-induced immuno-

suppression may lead to Strongyloides hyperinfection and dissemination with widespread larval migration, often accompanied by severe enterocolitis and potentially fatal gram-negative septicemia.

Corticosteroids should not be used in cerebral malaria.

Tuberculosis:

The use of prednisolone in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen.

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy these patients should receive chemoprophylaxis.

Vaccination:

Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered, however, the response to such vaccines can not be predicted. Immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g., for Addison's disease.

Ophthalmic:

Use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to bacteria, fungi or viruses. The use of oral corticosteroids is not recommended in the treatment of optic neuritis and may lead to an increase in the risk of new episodes. Corticosteroids should not be used in active ocular herpes simplex.

Cardio-renal:

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

PRECAUTIONS

General:

The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should be gradual.

Since complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment, a risk/benefit decision must be made in each individual case as to dose and duration of treatment and as to whether daily or intermittent therapy should be used.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy, most often for chronic conditions. Discontinuation of corticosteroids may result in clinical improvement.

Endocrine:
Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

Ophthalmic:
Intraocular pressure may become elevated in some individuals. If steroid therapy is continued for more than 6 weeks, intraocular pressure should be monitored.

Neuro-psychiatric:
Although controlled clinical trials have shown corticosteroids to be effective in speeding the resolution of acute exacerbations of multiple sclerosis, they do not show that they affect the ultimate outcome or natural history of the disease. The studies do show that relatively high doses of corticosteroids are necessary to demonstrate a significant effect. (See DOSAGE AND ADMINISTRATION.)

An acute myopathy has been observed with the use of high doses of corticosteroids, most often occurring in patients with disorders of neuromuscular transmission (e.g., myasthenia gravis), or in patients receiving concomitant therapy with neuromuscular blocking drugs (e.g., pancuronium). This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevation of creatinine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Gastrointestinal:
Steroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection: diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer.

Signs of peritoneal irritation following gastrointestinal perforation in patients receiving corticosteroids may be minimal or absent.

Cardio-renal:

As sodium retention with resultant edema and potassium loss may occur in patients receiving corticosteroids, these agents should be used with caution in patients with hypertension, congestive heart failure, or renal insufficiency.

Musculoskeletal:

Corticosteroids decrease bone formation and increase bone resorption both through their effect on calcium regulation (i.e., decreasing absorption and increasing excretion) and inhibition of osteoblast function. This, together with a decrease in the protein matrix of the bone secondary to an increase in protein catabolism, and reduced sex hormone production, may lead to inhibition of bone growth in children and adolescents and the development of osteoporosis at any age. Special consideration should be given to patients at increased risk of osteoporosis (i.e., postmenopausal women) before initiating corticosteroid therapy.

Information for Patients:

Patients should be warned not to discontinue the use of Prednisolone Sodium Phosphate Oral Solution abruptly or without medical supervision, to advise any medical attendants that they are taking Prednisolone Sodium Phosphate Oral Solution and to seek medical advice at once should they develop fever or other signs of infection.

Persons who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles. Patients should also be advised that if they are exposed, medical advice should be sought without delay.

Drug Interactions:

Drugs such as barbiturates, phenytoin, ephedrine, and rifampin, which induce hepatic microsomal drug metabolizing enzyme activity may enhance metabolism of prednisolone and require that the dosage of Prednisolone Sodium Phosphate Oral Solution be increased.

Increased activity of both cyclosporin and corticosteroids may occur when the two are used concurrently. Convulsions have been reported with this concurrent use.

Estrogens may decrease the hepatic metabolism of certain corticosteroids thereby increasing their effect.

Ketoconazole has been reported to decrease the metabolism of certain corticosteroids by up to 60% leading to an increased risk of corticosteroid side effects.

Coadministration of corticosteroids and warfarin usually results in inhibition of response to warfarin, although there have been some conflicting reports. Therefore, coagulation indices should be monitored frequently to maintain the desired anticoagulant effect.

Concomitant use of aspirin (or other non-steroidal anti-inflammatory agents) and corticosteroids increases the risk of gastrointestinal side effects. Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia. The clearance of salicylates may be increased with concurrent use of corticosteroids.

When corticosteroids are administered concomitantly with potassium-depleting agents (i.e., diuretics, amphotericin-B), patients should be observed closely for development of hypokalemia. Patients on digitalis glycosides may be at increased risk of arrhythmias due to hypokalemia.

Concomitant use of anticholinesterase agents and corticosteroids may produce severe weakness in patients with myasthenia gravis. If possible, anticholinesterase agents should be withdrawn at least 24 hours before initiating corticosteroid therapy.

Due to inhibition of antibody response, patients on prolonged corticosteroid therapy may exhibit a diminished response to toxoids and live or inactivated vaccines. Corticosteroids may also potentiate the replication of some organisms contained in live attenuated vaccines. If possible, routine administration of vaccines or toxoids should be deferred until corticosteroid therapy is discontinued.

Because corticosteroids may increase blood glucose concentrations, dosage adjustment of antidiabetic agents may be required.

Corticosteroids may suppress reactions to skin tests.

Pregnancy: Teratogenic Effects: Pregnancy Category C.

Prednisolone has been shown to be teratogenic in many species when given in doses equivalent to the human dose. Animal studies in which prednisolone has been given to pregnant mice, rats, and rabbits have yielded an increased incidence of cleft palate in the offspring. There are no adequate and well-controlled studies in pregnant women. Prednisolone Sodium Phosphate Oral Solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Infants born to mothers who have received corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Nursing Mothers:

Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Caution should be exercised when Prednisolone Sodium Phosphate Oral Solution is administered to a nursing woman.

Pediatric Use:

The efficacy and safety of prednisolone in the pediatric population are based on the well-established course of effect of corticosteroids which is similar in pediatric and adult populations. Published studies provide evidence of efficacy and safety in pediatric patients for the treatment of nephrotic syndrome (>2 years of age), and aggressive lymphomas and leukemias (>1 month of age). However, some of these conclusions and other indications for pediatric use of corticosteroid, e.g., severe asthma and wheezing, are based on adequate and well-controlled trials conducted in adults, on the premises that the course of the diseases and their pathophysiology are considered to be substantially similar in both populations.

The adverse effects of prednisolone in pediatric patients are similar to those in adults (see ADVERSE REACTIONS). Like adults, pediatric patients should be carefully observed with

frequent measurements of blood pressure, weight, height, intraocular pressure, and clinical evaluation for the presence of infection, psychosocial disturbances, thromboembolism, peptic ulcers, cataracts, and osteoporosis. Children who are treated with corticosteroids by any route, including systemically administered corticosteroids, may experience a decrease in their growth velocity. This negative impact of corticosteroids on growth has been observed at low systemic doses and in the absence of laboratory evidence of HPA axis suppression (i.e., cosyntropin stimulation and basal cortisol plasma levels). Growth velocity may therefore be a more sensitive indicator of systemic corticosteroid exposure in children than some commonly used tests of HPA axis function. The linear growth of children treated with corticosteroids by any route should be monitored, and the potential growth effects of prolonged treatment should be weighed against clinical benefits obtained and the availability of other treatment alternatives. In order to minimize the potential growth effects of corticosteroids, children should be *titrated* to the lowest effective dose.

ADVERSE REACTIONS

(listed alphabetically under each subsection)

Fluid and Electrolyte Disturbances: Congestive heart failure in susceptible patients; fluid retention; hypertension; hypokalemic alkalosis; potassium loss; sodium retention.
Cardiovascular: Hypertrophic cardiomyopathy in premature infants.
Musculoskeletal: Aseptic necrosis of femoral and humeral heads; loss of muscle mass; muscle weakness; osteoporosis; pathologic fracture of long bones; steroid myopathy; tendon rupture; vertebral compression fractures.
Gastrointestinal: Abdominal distention; elevation in serum liver enzyme levels (usually reversible upon discontinuation); pancreatitis; peptic ulcer with possible perforation and hemorrhage; ulcerative esophagitis.
Dermatologic: Facial erythema; increased sweating; impaired wound healing; may suppress reactions to skin tests; petechiae and ecchymoses; thin fragile skin; urticaria; edema.
Metabolic: Negative nitrogen balance due to protein catabolism.
Neurological: Convulsions; headache; increased intracranial pressure with papilledema (pseudotumor cerebri), usually following discontinuation of treatment; psychic disorders; vertigo.
Endocrine: Decreased carbohydrate tolerance; development of cushingoid state; hirsutism; increased requirements for insulin or oral hypoglycemic agents in diabetes; manifestations of latent diabetes mellitus; menstrual irregularities; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness; suppression of growth in children.
Ophthalmic: Exophthalmos; glaucoma; increased intraocular pressure; posterior subcapsular cataracts.
Other: Increased appetite; malaise; nausea; weight gain.

OVERDOSAGE

The effects of accidental ingestion of large quantities of prednisolone over a very short period of time have not been reported, but prolonged use of the drug can produce mental symptoms, moon face, abnormal fat deposits, fluid retention, excessive appetite, weight gain, hypertrichosis, acne, striae, ecchymosis, increased sweating, pigmentation, dry scaly skin, thinning scalp hair,

increased blood pressure, tachycardia, thrombophlebitis, decreased resistance to infection, negative nitrogen balance with delayed bone and wound healing, headache, weakness, menstrual disorders, accentuated menopausal symptoms, neuropathy, fractures, osteoporosis, peptic ulcer, decreased glucose tolerance, hypokalemia, and adrenal insufficiency. Hepatomegaly and abdominal distention have been observed in children.

Treatment of acute overdosage is by immediate gastric lavage or emesis followed by supportive and symptomatic therapy. For chronic overdosage in the face of severe disease requiring continuous steroid therapy the dosage of prednisolone may be reduced only temporarily, or alternate day treatment may be introduced.

DOSAGE AND ADMINISTRATION

The initial dose of Prednisolone Sodium Phosphate Oral Solution may vary from 5 to 60 mg prednisolone base per day depending on the specific disease entity being treated. In situations of less severity, lower doses will generally suffice while in selected patients higher initial doses may be required. The initial dosage should be maintained or adjusted until a satisfactory response is noted. If after a reasonable period of time, there is a lack of satisfactory clinical response, Prednisolone Sodium Phosphate Oral Solution should be discontinued and the patient placed on other appropriate therapy. **IT SHOULD BE EMPHASIZED THAT DOSAGE REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE DISEASE UNDER TREATMENT AND THE RESPONSE OF THE PATIENT.** After a favorable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small decrements at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. It should be kept in mind that constant monitoring is needed in regard to drug dosage. Included in the situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment; in this latter situation it may be necessary to increase the dosage of Prednisolone Sodium Phosphate Oral Solution for a period of time consistent with the patient's condition. If after long term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

In the treatment of acute exacerbations of multiple sclerosis daily doses of 200 mg of prednisolone for a week followed by 80 mg every other day or 4 to 8 mg dexamethasone every other day for one month have been shown to be effective.

In pediatric patients, the initial dose of Prednisolone Sodium Phosphate Oral Solution may vary depending on the specific disease entity being treated. The range of initial doses is 0.14 to 2 mg/kg/day in three or four divided doses (4 to 60 mg/m^2bsa/day).

The standard regimen used to treat nephrotic syndrome in pediatric patients is 60 mg/m^2/day given in three divided doses for 4 weeks, followed by 4 weeks of single dose alternate-day therapy at 40 mg/m^2/day.

The National Heart, Lung, and Blood Institute (NHLBI) recommended dosing for systemic *prednisone, prednisolone or methylprednisolone* in children whose asthma is uncontrolled by inhaled corticosteroids and long-acting bronchodilators is 1-2 mg/kg/day in single or divided doses. It is further recommended that short course, or "burst" therapy, be continued until a child achieves a peak expiratory flow rate of 80% of his or her personal best or symptoms resolve. This usually requires 3 to 10 days of treatment, although it can take longer. There is no evidence that tapering the dose after improvement will prevent a relapse.

For the purpose of comparison, 20.2 mg prednisolone sodium phosphate is equivalent to the following milligram dosage of the various glucocorticoids:

Cortisone, 75	*Triamcinolone, 12*
Hydrocortisone, 60	*Paramethasone, 6*
Prednisolone, 15	*Betamethasone, 2.25*
Prednisone, 15	*Dexamethasone, 2.25*
Methylprednisolone, 12	

These dose relationships apply only to oral or intravenous administration of these compounds. When these substances or their derivatives are injected intramuscularly or into joint spaces, their relative properties may be greatly altered.

HOW SUPPLIED

Prednisolone Sodium Phosphate Oral Solution (eq. 10 mg prednisolone base): Each 5 mL (teaspoonful) of flavored solution contains 13.5 mg prednisolone sodium phosphate (10 mg prednisolone base).
Available as
□ fl oz (□ mL) NDC XXXXX-XXX-XX

Prednisolone Sodium Phosphate Oral Solution (eq. 20 mg prednisolone base): Each 5 mL (teaspoonful) of flavored solution contains 26.9 mg prednisolone sodium phosphate (20 mg prednisolone base).
Available as:
□ fl oz (□ mL) NDC XXXXX-XXX-XX

Prednisolone Sodium Phosphate Oral Solution (eq. 25 mg prednisolone base): Each 5 mL (teaspoonful) of flavored solution contains 33.7 mg prednisolone sodium phosphate (25 mg prednisolone base).
Available as:
□ fl oz (□ mL) NDC XXXXX-XXX-XX

Dispense in tight, light-resistant glass or PET plastic containers as defined in USP.

Store refrigerated, 2-8°C (36-46°F)
Keep tightly closed and out of the reach of children.

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